

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/051170

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/68 G01N33/92 C12Q1/68 A61K31/00 A61K38/00
A61K39/00
//C07K14/775

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N C12Q A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, WPI Data, EMBASE, BIOSIS, COMPENDEX

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>LINGAPPA VR ET AL: "Translocational pausing and the regulation of membrane protein biogenesis"</p> <p>MEMBRANE PROTEINS: STRUCTURE, FUNCTION AND EXPRESSION CONTROL KYUSHU UNIVERSITY PRESS, 7-1-146, HAKOZAKI, HIGASHI-KU, FUKUOKA 812, JAPAN; S. KARGER AG, P.O. BOX, ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND, 1997, pages 93-100, XP001183818</p> <p>& INTERNATIONAL SYMPOSIUM ISSN: 3-8055-6465-1 page 95, paragraph 4 - page 97, paragraph 2; figure 2</p> <p style="text-align: center;">----- -/-</p>	1-28



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

6 October 2004

Date of mailing of the international search report

02/11/2004

Name and mailing address of the ISA

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CLAVEY V ET AL: "INTERACTION ENTRE LE LDL-RECEPTEUR ET LES LIPOPROTEINES CONTENANT DE L'APO B INTERACTION BETWEEN THE LDL RECEPTOR AND THE LIPOPROTEINS CONTAINING APOB" ANNALES D'ENDOCRINOLOGIE, MASSON, PARIS, FR, vol. 52, no. 6, 1991, pages 459-463, XP001029770 ISSN: 0003-4266 cited in the application abstract	1-28
Y	BAUMANN, MARC H. ET AL: "Apolipoprotein E includes a binding site which is recognized by several amyloidogenic polypeptides" BIOCHEMICAL JOURNAL, vol. 349, no. 1, 1 July 2000 (2000-07-01), pages 77-84, XP002262330 cited in the application abstract; figures 2,4 page 78, column 1, paragraph 4	1,3
Y	WO 02/065133 A (SALAMA ABDULGABAR; KIESEWETTER HOLGER (DE)) 22 August 2002 (2002-08-22) cited in the application abstract; claim 1; examples 11-13	1,3
Y	WO 03/005037 A (STEFAS ELIE ;APOH TECHNOLOGIES SA (FR)) 16 January 2003 (2003-01-16) cited in the application page 2, line 19 - line 26 abstract; claims 1-3	1,3
X	US 2002/155426 A1 (BALES KELLY R ET AL) 24 October 2002 (2002-10-24) cited in the application abstract; claims 1,4,22,23 paragraphs '0009!, '0055!	2-6,9-14
A	WO 97/14437 A (WEISGRABER KARL H ;MAHLEY ROBERT W (US); PITAS ROBERT E (US); UNIV) 24 April 1997 (1997-04-24) cited in the application abstract; claims 1,2,7,11-14 page 5, line 5 page 11, line 7 - line 20 page 13, line 1 - line 20 page 21, line 7 - line 16	9-14
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 99/15159 A (NOVA MOLECULAR INC) 1 April 1999 (1999-04-01) cited in the application abstract; claims 1,17,19,24,31,32,36 -----	9-14
A	US 6 462 171 B1 (SOTO-JARA CLAUDIO ET AL) 8 October 2002 (2002-10-08) abstract; claims 1,3,5,13,15 column 13, line 45 - line 58 -----	9-14
A	US 6 022 683 A (POIRIER JUDES) 8 February 2000 (2000-02-08) cited in the application abstract; claims 1-4,13,14 column 3, line 4 - line 8 column 3, line 59 - line 63 column 6, line 7 - line 16 -----	16-18,28
A	DIEDRICH, JANE F. ET AL: "Neuropathological changes in scrapie and Alzheimer's disease are associated with increased expression of apolipoprotein E-- and cathepsin D in astrocytes" JOURNAL OF VIROLOGY, vol. 65, no. 9, September 1991 (1991-09), pages 4759-4768, XP000443989 cited in the application abstract page 4759, column 2, line 5 - line 10 page 4764, column 2; figures 3,4 -----	16-18,28
A	CHOE, LEILA H. ET AL: "Apolipoprotein E and other cerebrospinal fluid proteins differentiate ante mortem variant Creutzfeldt-Jakob disease from ante mortem sporadic Creutzfeldt-Jakob disease" ELECTROPHORESIS, vol. 23, no. 14, 14 July 2002 (2002-07-14), pages 2242-2246, XP002262331 cited in the application abstract page 2242, column 1, paragraph 1 - column 2, paragraph 1 page 2244, column 2, paragraph 2 -----	16-18,28
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>GOLAZ OLIVIER ET AL: "Phenotyping of apolipoprotein E using immobilized pH gradient gels for one-dimensional and two-dimensional separations" ELECTROPHORESIS, vol. 16, no. 7, 1995, pages 1184-1186, XP009021630 ISSN: 0173-0835 cited in the application abstract</p>	16-18,28
A	<p>LUCASSEN RALF ET AL: "In vitro amplification of protease-resistant prion protein requires free sulfhydryl groups" BIOCHEMISTRY;BIOCHEMISTRY APR 15 2003, vol. 42, no. 14, 15 April 2003 (2003-04-15), pages 4127-4135, XP002262517 cited in the application abstract</p>	1-8
A	<p>ENARI M FLECHSIG E WEISSMANN C: "Scrapie prion protein accumulation by scrapie-infected neuroblastoma cells abrogated by exposure to a prion protein antibody" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 98, no. 16, 31 July 2001 (2001-07-31), pages 9295-9299, XP002959455 ISSN: 0027-8424 cited in the application abstract</p>	1-8
P,A	<p>US 2004/018554 A1 (GREEN LARRY R) 29 January 2004 (2004-01-29) abstract; claims 13-15</p>	1-8

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claims 15 to 18 are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box II.2

Claims Nos.: 12,22,26

Present claims 12, 22 and 26 relate to an extremely large number of possible use/method/assay. In fact, the claims contain so many options and variables that a lack of clarity (and conciseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claim impossible. Moreover, there is no SEQ ID provided for the fragments of the sequences disclosed in said claims 12, 22 and 26 (Rule 5.2 PCT), and said fragments are defined by reference to a parameter ("is of a molecular weight selected from 30 and 40 kDa). The use of this parameters in the present context is considered to lead to a lack of clarity within the meaning of Article 6 PCT. It is impossible to compare the parameters the applicant has chosen to employ with what is set out in the prior art. The lack of clarity is such as to render a meaningful complete search impossible.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 15-18
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 15 to 18 are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 12, 22, 26
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 02065133	A	22-08-2002	DE 10107083 A1 WO 02065133 A2 EP 1360502 A2 JP 2004518966 T US 2004096902 A1	29-08-2002 22-08-2002 12-11-2003 24-06-2004 20-05-2004
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WO 9714437	A	24-04-1997	AU 718498 B2 AU 5297696 A CA 2233848 A1 EP 0862460 A1 JP 2001517198 T WO 9714437 A1 US 2002009439 A1	13-04-2000 07-05-1997 24-04-1997 09-09-1998 02-10-2001 24-04-1997 24-01-2002
WO 9915159	A	01-04-1999	AU 9454098 A CA 2304505 A1 EP 1017375 A2 WO 9915159 A2 JP 2001517617 T US 6274603 B1 US 2001051602 A1	12-04-1999 01-04-1999 12-07-2000 01-04-1999 09-10-2001 14-08-2001 13-12-2001
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US 6022683	A	08-02-2000	AT 269978 T AU 5571798 A AU 745073 B2 AU 5675798 A CA 2275404 A1 CA 2275504 A1 DE 69729473 D1 DE 69729654 D1 EP 0948647 A1 EP 0946753 A2 WO 9827226 A2 WO 9827227 A2 JP 2001524809 T	15-07-2004 15-07-1998 14-03-2002 15-07-1998 25-06-1998 25-06-1998 15-07-2004 29-07-2004 13-10-1999 06-10-1999 25-06-1998 25-06-1998 04-12-2001

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2004018554	A1	29-01-2004	NONE